from those caused by bacterial agency. They compose a fairly large share of the cases of chronic progressive arthritis seen in the daily routine of practice. A general flaccidity of tissues and relaxation of important organs accompanied by ptosis of the abdominal viscera often characterize these cases.

In acute arthritis the probability of producing a cure or improvement by the removal of a supposed focus in the teeth or tonsils is greater than in cases in the chronic stage. It is unreasonable to suppose that a restoration of function can be brought about in joints where extensive pathological changes have taken place.

One very suggestive fact brought out in this investigation has been the marked improvement in the general health of the patients when diseased conditions of the teeth and tonsils have been properly treated. It oftentimes seems as if a millstone had been removed from their necks. This is noted very commonly even when no change was apparent in the joint condition.

EXPERIMENTAL LESIONS IN THE CERVICAL SYMPATHETIC GANGLIA IN RELATION TO EXOPHTHALMIC GOITER.[1]

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That exophthalmic goiter, the clinical manifestations of which are due essentially to a greatly increased protein metabolism, is the joint result of disturbance in the several glands concerned with metabolism there can be little doubt. The fact that the thyroid shows a pronounced and constant series of functional changes parallel with the course of the disease and the further fact that removal of the gland arrests the symptoms is convincing though not absolute proof that the thyroid is the secretory gland the hyperfunction of which initiates the metabolic disturbance.

But is the primary hyperfunction of the thyroid the result of primary pathological change within the gland itself or of direct stimulation from its nerve supply? Cannon's[2] experimental production in cats of some of the symptoms of exophthalmic goiter by continuous stimulation of the thyroid through the sympathetic system suggests the latter. Durante and I[3] have shown that in all cases of exophthalmic goiter we have had an opportunity to examine there is a pronounced and constant pathological lesion in the cervical sympathetic ganglia from which the thyroid receives its entire nerve supply. There is much suggestive evidence that these pathological changes in the cervical sympathetic ganglia are the result of direct bacterial infection within the ganglia.

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[1] Presented before the Association of American Physicians, Atlantic City, N. J., May 3, 1917.

[2] Cannon, W. B., Binger, C. A. L., and Fitz, R.: Experimental Hyperthyroidism, Am. Jour. Physiol., 1914–15, xxxvi, 363-364.

[3] Wilson, L. B., and Durante, L.: Changes in the Superior Cervical Sympathetic Ganglia Removed for the Relief of Exophthalmos, Jour. Med. Research, 1916, N. S., xxxiv, 273-296. Wilson, L. B.: The Pathological Changes in the Sympathetic System in Goiter, Am. Jour. Med. Sc., 1916, clii, 799-812. Wilson, L. B.: Further Study of the Histopathology of the Autonomic Nervous System in Goiter, Jour. Lab. and Clin. Med., 1917, ii, 295-307.

The object of the present series of experiments has been to determine the effect directly upon the cervical sympathetic ganglia and indirectly upon the thyroid of various forms of stimulation applied to the ganglia themselves in healthy animals. Goats have been used for the experiments almost exclusively, and the results on these animals only will be described herein. The goat is a very desirable animal for experiments on the sympathetic ganglia and the thyroid, since the tissue elements of both these organs in their normal and pathological morphology and their staining reactions closely resemble those of the tissue elements of the same organs in man.

Stimulation in some of the experiments has been produced by electricity; in most instances, however, the stimulus has been obtained by direct bacterial inoculation into the ganglia. Observations have been completed on nineteen goats, and are still in progress on six others.

TECHNIC. *Electric Stimulation.* After proper etherization of a goat its right superior cervical sympathetic ganglion was exposed. The ganglion was then directly stimulated by a moderate tetanizing current for one second, at intervals of three seconds, for a period of one hour. During the experiment the animal's blood-pressure was taken and the amount of saliva excreted noted. After one hour the right cervical ganglion and the right lobe of the thyroid were removed with as little loss of blood as possible. The left superior cervical sympathetic ganglion was then exposed and stimulated in the same manner as the right had been, but for a period of five and a half hours. At the end of five and a half hours the left superior cervical sympathetic ganglion and the left lobe of the thyroid were removed. After removal the ganglia and the lobes of the thyroids were properly fixed and stained by various methods, the ganglia usually by Nissl's and Ramon y Cajal's methods and the thyroid with hematoxylin-eosin and by Bensley's acid-fuchsin-methylene-green after acetic-osmic-bichromate fixation.

Bacterial Stimulation. After properly etherizing a goat its right or left superior cervical sympathetic ganglion was exposed and a small quantity of a culture of some bacterium was injected into the capsule of the ganglion. The wound was closed with aseptic precautions and the goat placed under observation. The period of observation varied from three days to three months. A few of the animals died and in such instances complete postmortems were made. In some of the others the cervical sympathetic ganglia and the lobes of the thyroid from both sides were removed at operations. In the remainder of the goats only the injected ganglion and the thyroid lobe on the same side were removed and examined.

SUMMARY OF OBSERVATIONS. 1. The normal nerve cells of the cervical sympathetic ganglia in the adult goat closely resemble the normal nerve cells of the cervical sympathetic ganglia of the human adult, except that a relatively large number of them are binucleate. Similarly, the thyroid of the adult goat when at rest histologically closely resembles the resting adult human thyroid.

2. (*a*) Moderate electrical stimulation applied for one second at intervals of three seconds for a period of one hour to the superior cervical sympathetic ganglion of an adult goat appears to produce no marked changes in the blood-pressure or respiration. If there were any definite changes they were masked by the diffuse stimulation involving the vagus. There was marked salivation.

(*b*) Microscopically, after the electrical stimulation noted above a large number of the nerve cells of the stimulated ganglion were swollen and showed hyperchromatization. The demonstration of dissolution of the chromatin by Nissl's method or of the presence of lipoid changes by Sudan III and Ramon y Cajal's methods has not been possible in any of the cells.

(*c*) After the above-mentioned stimulation the cells of the thyroid parenchyma were found swollen, their protoplasm distinctly granular and their nuclei well rounded. The acini were distended with a feebly staining secretion, the numerous large vacuoles in stained preparations of which indicated the liquid character of the secretion. The condition of the cells and colloid secretion was parallel in all respects to that found in the thyroids of early cases of exophthalmic goiter in the human subject.

3. (*a*) Moderate electrical stimulation applied to the superior cervical sympathetic ganglion for one second, at intervals of three seconds, throughout a period of five and a half hours, produced clinical changes similar to those noted in Paragraph 2.

(*b*) Microscopically, after the electrical stimulation noted above, many of the nerve cells were markedly swollen and showed intense hyperchromatization. Many were swollen, hydropic and with disseminated chromatin. Sudan III preparations, even when thoroughly differentiated, showed conclusive evidence of lipoid change. This was demonstrated by Ramon y Cajal's method.

(*c*) After the above-mentioned stimulation the cells of the thyroid parenchyma were found swollen but not nearly so much so as in those thyroids in which stimulation had been applied for only one hour. The protoplasm was clear and the nuclei showed a tendency to crenation. The acini were usually more distended and were filled with colloid material, which was more densely stained and contained fewer vacuoles than that noted in Paragraph 2 (*b*). These changes were evidently the result of beginning exhaustion of the cells and resembled the changes in the thyroid in cases of exophthalmic goiter in the human subject in which remission of symptoms has already begun.

4. (*a*) After the injection of a virulent culture of Streptococcus hemolyticus into the capsule of the superior cervical sympathetic ganglion of goats the animals died within three days after exhibiting symptoms of an intense toxemia.

(*b*) Within the injected ganglion of such a goat the nerve cells were found to lie in greatly distended pericellular lymph spaces. They were markedly hyperchromatic and hydropic, with diffuse dissemination of the chromatin, or were more or less completely disintegrated. No evidence of lipoid change was demonstrated by the Sudan III or silver-impregnation methods.

(*c*) After the above injection the cells of the thyroid parenchyma were palely staining, not swollen and apparently not overfunctioning. The amount and character of the colloid within the acini was not distinguishable from normal.

5. After the injection of certain strains of Bacillus influenzæ of apparently low virulence no systemic reaction or histological lesions were demonstrated. After the injection of other strains more recently isolated a marked inflammatory reaction was found around the injected ganglia, though the goats had shown no symptoms. Changes within the ganglia and within the thyroid were indistinguishable from those within the ganglia and thyroids from the goats described in Paragraph 6.

6. (*a*) The injection of freshly isolated virulent cultures of Bacillus bronchisepticus into the superior cervical sympathetic ganglion of adult goats usually produced marked constitutional symptoms such as trembling, increase of temperature, and loss of appetite, and frequently caused death in from three days to three weeks. No exophthalmos was noted.

(*b*) Within the injected ganglion of such a goat many of the nerve cells in animals dying early were found to be markedly hyperchromatic; others were hydropic, with disseminated or invisible chromatin and more or less distorted nuclei within such cells. Sudan III and silver-impregnation preparations showed the presence of changed lipoids. In the ganglia of goats that lived three weeks or more there was unmistakable evidence of complete cell destruction, in some instances extending from the point of inoculation well into the ganglion. Lipoid pigmentation was distinctly shown by Sudan III and silver impregnation. Histologically, these changes were parallel to those found in the ganglia in cases of exophthalmic goitre in the human subject.

(*c*) In goats from which the thyroid had been removed in from three days to three weeks after the injection the cells of the thyroid parenchyma were actively functionating, as was evidenced by their swollen size, granular protoplasm, well-rounded nuclei and the presence of large quantities of feebly staining secretion within the acini. The histological appearance was closely parallel with that found in the thyroid in early cases of exophthalmic goiter. When a period of three months had elapsed between inoculation and removal of the thyroid the thyroid parenchyma showed evidence of exhausted function in that the cells were no longer swollen, their nuclei were more or less crenated and the colloid secretion within the acini was densely staining.

CONCLUSION. From the above experiments it would appear that irritation from the presence of certain bacteria within the cervical sympathetic ganglia of the goat may produce histological pictures within the ganglia and in the thyroid which parallel those found in the various stages of progressive and regressive exophthalmic goiter. This evidence supports the suggestion that in exophthalmic goiter the thyroid receives its stimulus to overfunction through its nerve supply and as a result usually of a local infection in the cervical sympathetic ganglia.

A STATISTICAL STUDY OF THE RELATIONSHIP OF THE ORIGIN OF ECTOPIC CONTRACTIONS TO VENTRICULAR PREPONDERANCE AS SHOWN BY THE ELECTROCARDIOGRAPH.[1]

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THAT the form of the electrocardiogram may indicate relative ventricular preponderance has been known for some time, but the relationship of such preponderance to the origin of ectopic contractions has, so far as we are aware, never been made a subject of study. Is it not possible that there may be some underlying relationship between preponderance and ectopic contractions that has escaped our attention up to the present?

It was with this possibility in mind that we began the review of the 375 cases studied by means of the electrocardiograph within the past eighteen months. The study was made in the cardiographic laboratory of the University of Pittsburgh, School of Medicine, at St. Francis Hospital. Most of the electrocardiograms were taken on patients who presented some cardiac disturbance, although a few were taken on patients in whom no cardiac lesion was suspected.

In the determination of preponderance we have used the criteria of Lewis,[2] slightly modified. Lewis, following the teachings of

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[1] R. B. Mellon Fellow in Internal Medicine, University of Pittsburgh, School of Medicine, Pittsburgh, Pa.

[2] Clinical Electrocardiography, Shaw & Sons, London, 1913. Observations upon Ventricular Hypertrophy, with Special Reference to Preponderance of One or Other Chamber, Heart, 1914, No. 4, v, 367–402.